When do you step up or increase long-term control medications?

To regain control when the child has:

- Increased symptoms and/or nighttime awakenings due to symptoms.
- Reduced ability to play, exercise, or participate in normal daily activities.
- Daily or increasing use of short-acting beta₂-agonists.
- Reduction in PEF (by about 20%).
- When the goals of therapy are not being achieved.

How to help the child regain control of asthma:

- A short (3- to 10-day) course of oral corticosteroids may be needed to speed the resolution of moderate or severe exacerbations, or to reestablish control during a period of gradually deteriorating symptoms.
- If a short course of oral corticosteroids does not control symptoms, is effective for only a short time (i.e., < 2 weeks), or if the child used oral corticosteroids frequently, consider a step-up or increase in the longterm control medication. This can be achieved by:
 - \Rightarrow Increasing the dose.
 - \Rightarrow Increasing the frequency of dosing.
 - \Rightarrow Using or adding a different medication.



Before increasing medications, assess possible reasons for poor asthma control:

- Inhaler technique
- Adherence
- Environmental exposures
- Complicating factors (e.g., upper respiratory infections)

Remember the goals of therapy:

- Prevent chronic and troublesome symptoms.
- Prevent exacerbations of symptoms.
 - ⇒ No acute episodes of asthma that require a doctor visit, emergency room visit, or hospital stay.
- Maintain normal activity levels.
- Maintain "normal" pulmonary function.
- Minimal (ideally no) adverse effects from medication.

Children with severe persistent asthma may need to use oral corticosteroids on a long-term basis.

Children with asthma whose symptoms are not controlled on high doses of inhaled corticosteroids *and* long-acting bronchodilators may need to use oral corticosteroids on a regular, long-term basis. For these children:

- Use the lowest possible dose (single dose, daily or on alternate days).
- Monitor the child closely for corticosteroid adverse effects.
- Make persistent attempts to reduce use of oral corticosteroids when control of asthma is achieved. High doses of inhaled corticosteroids are preferable because of fewer adverse effects.
- Regular consultation with an asthma specialist is recommended.

Remember when using the stepwise approach to therapy that referral to an asthma specialist for consultation or co-management is recommended when:

- The child has had a life-threatening asthma exacerbation.
- Goals of asthma therapy are not being met after 3-6 months of treatment; earlier if the child appears unresponsive to treatment.
- Signs and symptoms are atypical, or there are problems in differential diagnosis.
- Other conditions complicate asthma or its diagnosis (e.g., untreated sinusitis, rhinitis).
- Additional diagnostic testing is indicated (e.g., pulmonary function testing, allergy skin testing).
- The child or family needs additional education and guidance on complications of therapy, problems with adherence, or avoidance of triggers.
- The child is being considered for immunotherapy.
- The child has severe persistent asthma.
- The child is under 3 years of age and has moderate or severe persistent asthma.
- The child has used long-term oral corticosteroid therapy, high-dose inhaled corticosteroid therapy, or more than 2 bursts of oral corticosteroids in 12 months.

Treat asthma exacerbations promptly and aggressively.

- All children with asthma need an inhaled, short-acting beta₂-agonist (MDI, nebulizer, DPI) for exacerbations.
- Give the child, the child's family, and caregivers (daycare providers, teachers, coaches, scout leaders, camp counselors, school and camp nurses) a written, easy-to-understand ACTION PLAN to manage exacerbations. Include:
 - ⇒ The early signs of worsening asthma.
 - ⇒ Which medications to use and how to use them.
 - ⇒ Specific instructions for when to contact the physician or emergency room.
- A short (3- to 10-day) course of oral corticosteroids may be needed to speed the resolution of moderate persistent or severe persistent exacerbations, or to reestablish control during a period of gradually deteriorating symptoms.
- Exacerbations of asthma symptoms (coughing, wheezing, shortness of breath or rapid breathing, chest tightness) with viral respiratory infections are common in children, and need to be treated appropriately with adequate doses of short-acting beta₂-agonists and, in some cases, oral corticosteroids.
- Asthma exacerbations may require treatment at the physician's office or emergency room.
 - ⇒ Frequent short-acting beta₂-agonist, by nebulization.
 - ⇒ Consider adding ipratropium bromide.
 - ⇒ Consider oxygen to relieve hypoxemia.
 - ⇒ Pulse oximetry is recommended to follow oxygen saturation.
 - → Monitor the response to therapy with serial measurements of FEV₁ or PEF.

All children with asthma should have a short-acting bronchodilator to provide prompt relief of acute symptoms (coughing, wheezing, difficulty breathing, chest tightness).

Over-the-counter MDIs are not as effective as short-acting, inhaled beta₂-agonists, and may unnecessarily delay seeking medical care.

All offices that treat acute exacerbations of asthma should have a peak flow meter, a nebulizer, an oximeter, and oxygen.

Assessing the Severity of an Asthma Exacerbation

Asthma severity is a continuum. Any child, regardless of overall severity, can have a severe exacerbation.

Risk Factors for Death from Asthma

- Past history of sudden severe exacerbations
- Prior intubation for asthma
- Prior admission to intensive care unit for asthma
- ≥ 2 hospitalizations for asthma in past 12 months
- ≥ 3 emergency care visits for asthma in past 12 months
- Hospitalization or emergency care visit for asthma in past month
- Use of > 1 canister/month of inhaled short-acting beta,-agonist
- Current chronic use of oral corticosteroids
- Difficulty perceiving airflow obstruction or its severity
- Low socioeconomic status and urban residence
- Illicit drug use
- Serious psychiatric disease or psychosocial problems

Look at the child for signs of distress:

- Shortness of breath or rapid breathing
 - ⇒ As severity increases, the child may have difficulty talking or laying down. The infant may have difficulty feeding and may have a shorter, softer cry.
- Increased respiratory rate (see table below)
- Use of accessory muscles with retractions
- Wheezing
 - ⇒ In mild exacerbations, wheezing is evident on expiration.
 - ⇒ As the severity of the exacerbation increases, both inspiratory and expiratory wheezing may be present.
 - ⇒ During a severe exacerbation, the chest may be "silent."
- Decreased PEF
- Agitation

Normal Breathing and Pulse Rates for Children

Age	Breathing rate (awake)	Pulse rate
< 2 months	< 60/minute	< 160/minute
2-12 months	< 50/minute	< 120/minute
12-24 months	< 40/minute	< 110/minute
2-5 years	< 40/minute	< 110/minute
6-8 years	< 30/minute	< 110/minute

Managing Asthma Exacerbations in the Home

Assess severity

Measure PEF: < 50% predicted or personal best suggests severe exacerbation.

Note signs and symptoms: Degree of cough, shortness of breath, wheeze, chest tightness correlate imperfectly with severity. Accessory muscle use and retractions (sucking in of chest) suggest severe exacerbation.



Initial treatment

Inhaled short-acting beta₂-agonist: up to 3 Tx of 2-4 puffs by MDI every 20 min, or 1 nebulizer Tx



Repsonse to treatment	Good	Incomplete	Poor
Exacerbation PEF (predicted or personal best) Wheezing or shortness of breath	Mild > 80% None	Moderate 50%-80% Persistent	Severe < 50% Marked
Continued Treatment	Continue inhaled, short-acting beta ₂ - agonist every 3-4 hrs for 24-48 hrs. For children on inhaled corticosteroids, double dose for 7-10 days.	Continue inhaled short-acting beta ₂ - agonist. Add oral corticosteroid.	Repeat beta ₂ - agonist immediately. Add oral corticosteroid.
Follow-up	Contact clinician.	Contact clinician same day.	If distress is severe and child is non-responsive, CALL DOCTOR IMMEDIATELY, AND PROCEED TO EMERGENCY DEPARTMENT. CONSIDER CALLING AMBULANCE OR 911.

Management of Asthma Exacerbations: Emergency Department and Hospital-Based Care

Initial Assessment: History, physical examination (auscultation, use of accessory muscles, heart rate, respiratory rate), PEF or FEV₁, oxygen saturation, and other tests as indicated. FEV, or PEF < 50% (Severe **FEV**, or **PEF** > 50% **Impending or actual respiratory Exacerbation**) Inhaled beta₂-agonist by metered-dose arrest inhaler or nebulizer, up to 3 doses in first hour Inhaled, high-dose beta agonist and Intubation and mechanical anticholinergic by nebulization every 20 Oxygen to achieve 0₂ saturation ≥ 90% ventilation with 100% 0₃ Oral corticosteroids if no immediate minutes or continuously for 1 hour Nebulized beta, agonist and Oxygen to achieve 0_{\circ} saturation $\geq 90\%$ response or if patient recently took anticholinergic Oral corticosteroid oral corticosteroid Intravenous corticosteroid **Admit to Hospital Intensive Care Repeat Assessment**: Symptoms, physical examination, PEF, 0, saturation, other tests as needed (see below) **Severe Exacerbation Moderate Exacerbation** FEV, or PEF < 50% predicted/personal best FEV, or PEF 50%-80% predicted/personal best Physical exam: severe symptoms at rest, accessory muscle Physical exam: moderate symptoms use, chest retraction Inhaled short-acting beta_a-agonist every History: high-risk patient 60 minutes No improvement after initial treatment Systemic corticosteroid Inhaled short-acting beta agonist hourly or continuous Continue treatment 1-3 hours, provided plus inhaled anticholinergic there is improvement Oxvaen Systemic corticosteroid **Incomplete Response** FEV, or PEF \geq 50 but < 70% **Good Response** Mild-to-moderate symptoms **Poor Response** • FEV, or PEF ≥ 70% • FEV, or PEF < 50% Response sustained 60 minutes after last $PCO_2 \ge 42 \text{ mm Hg}$ treatment Individualized decision re: Physical exam: symptoms No distress hospitalization severe, drowsiness, confusion Physical exam: normal **Discharge Home** Admit to Hospital Ward **Admit to Hosptial Intensive Care** • Continue treatment with inhaled beta,-agonist Inhaled high-dose beta,-agonist plus Inhaled high-dose beta₂-agonist Continue course of oral corticosteroid hourly or continuously plus inhaled inhaled anticholinergic Patient education Systemic (oral or intravenous) anticholinergic ⇒ Review medicine use corticosteroid Intravenous corticosteroid ⇒ Review/initiate action plan **Oxygen Oxygen** ⇒ Recommend close medical follow-up Monitor FEV, or PEF, 0, saturation, pulse Possible intubation and mechanical ventilation **Improve**

Special Considerations when Treating Children with Asthma

Administering asthma medications to infants and children can be challenging.

- Medications to treat asthma in children may be given by inhalation or orally (as tablets or liquids).
 - ⇒ The inhaled route is generally preferred because:
 - Higher concentrations can be delivered more effectively to the airways.
 - Systemic side effects are avoided or minimized.
 - The onset of action of short-acting beta₂-agonists is substantially shorter when inhaled.
- Dosages reaching the airway will vary considerably depending on the route of administration (and the device(s) used for inhaled medications).
- The ability of individual children to use different devices for inhaled medications may vary considerably.

For children < 2 years:

- Nebulizer therapy with face mask may be preferred for administering cromolyn sodium, and for short-acting beta₂-agonists during exacerbations.
- Short-acting beta₂-agonists are available as liquids, but:
 - ⇒ The onset of action is slower than when given by inhalation (approximately 30 minutes for the liquid as compared to several minutes for inhalation).
 - ⇒ Adverse effects (e.g., tremor, irritability) are more likely.
- Drugs administered by MDI may be given using a spacer/holding chamber and face mask.
 - \Rightarrow The dose will be variable.
 - ⇒ Inhaled corticosteroids by MDI should always be given with a spacer/holding chamber.

How do you give medication to infants and young children?

- Use a metered dose inhaler with a spacer/ holding chamber plus face mask.
- Use a nebulizer.
- Use a liquid.

Liquid albuterol does not have as quick an onset-ofaction as inhaled albuterol, a consideration for treating exacerbations. Tailor the delivery device to the child, taking the child's needs into consideration.

For children between 3 and 5 years:

- Inhaled medications are preferred.
- Some children can use an MDI and spacer/holding chamber.
- If the desired therapeutic effects are not achieved, or if the child cannot use an MDI with spacer/holding chamber, a nebulizer or MDI plus spacer/holding chamber with face mask may be required.

For school-age children:

- Inhaled medications are preferred.
- MDIs, DPIs, and nebulizers may be used.
- The child should be able to produce the necessary effort and coordination needed for the specific device.
- All inhaled corticosteroids by MDI should be used with a spacer/holding chamber.
- Some children carry their short-acting beta₂-agonist MDI without a spacer/holding chamber. This is acceptable if the child has demonstrated good technique.
- School medication policies should be known.



Types of Inhalation Devices for Asthma Medications

Device/Medications	Age ¹	Comments
Metered-dose inhaler (MDI) Beta ₂ -agonists Corticosteroids Cromolyn sodium Nedocromil sodium Anticholinergics	> 5 years (< 5 years with spacer/holding chamber and face mask for some children)	The child may have difficulty triggering a puff while inhaling. Use with a spacer/holding chamber helps.
Breath-actuated MDI Beta ₂ -agonists	> 5 years	The child may not be able to generate the necessary inspiratory flow. Device does not require the use of holding chamber or spacer.
Dry-powder inhaler (DPI) Beta ₂ -agonists Corticosteroids	> 5 years (can be used in 4 year olds, but delivery is more consistent over 5)	Some devices deliver drug more effectively than an MDI. Some devices may not work in children with low inspiratory volumes.
Nebulizer Beta ₂ -agonists Cromolyn sodium Anticholinergics	Patients of any age who cannot use an MDI with spacer/holding chamber or with face mask.	Useful in infants and very young children, and any child with a moderate to severe asthma episode. Delivery method of choice for cromolyn sodium.

¹These ages are suggested as guides for making clinical decisions. The clinician must use his/her judgment to tailor treatment to the specific needs and circumstances of the child and family.

Using an MDI with a spacer/holding chamber may be easier than using an MDI alone.

- Trigger 1 puff from MDI into spacer/holding chamber for each inhalation.
- Some young children may be able to use an MDI with spacer/holding chamber and face mask.
 - ⇒ If a face mask is used, allow 3 to 5 inhalations for each puff triggered from the MDI.

Advantages of using spacers and holding chambers:

- Many children have a difficult time inhaling while pressing the inhaler to trigger a puff. Simple tubes do not take care of this problem!
- Decreases oropharyngeal deposition.
- Reduces possible side effects, particularly with inhaled corticosteroids.
 - ⇒ Potential side effects of inhaled corticosteroids include oral candida (thrush), dysphonia, and reflex cough and bronchospasm (also evident with other inhaled medications).

Instruct the child and parent in the appropriate use of all medications and devices. Advise the parent to share this information with ALL caregivers.

Have the child (and parent) bring and demonstrate use of their delivery devices (including inhalers, spacer/ holding chambers, face masks, nebulizers) at each office visit.

The child's schedule and giving asthma medications

- Provide an action plan for handling exacerbations, including the clinician's recommendation regarding self-administration of medication and plans to ensure prompt, reliable access to medications.
- If possible, schedule long-term control medications so that they are not taken at school, even if this results in uneven dosing intervals.
 - ⇒ However, some children benefit from close supervision of therapy. For these children, giving medication at school, under the supervision of a school health professional, is recommended.
- It may be helpful for some younger children to have a compressor-driven nebulizer available at their school or daycare facility.

Reliable, prompt access to asthma medication is essential during the day.

- The child, caregivers, teachers, school nurses, and school boards should understand this.
- Older children should be allowed to carry and selfadminister quick-relief medications, with physician and parent approval.



Infants and adolescents have special needs.

0 to 18 months

- Early management of wheezing may alter the course of asthma later on. However, infants can be difficult to manage. Referral to a pediatric asthma specialist for consultation or co-management should be considered for children being given daily medication.
- Carefully monitor the response to medication.
 - ⇒ Treat the wheeze for 4 to 8 weeks.
 - ⇒ If there is no clear response, stop treatment.
 - ⇒ Consider alternate therapy or an alternate diagnosis if the child is not: growing and developing normally, eating normally and gaining weight, or sleeping.
- Diet is usually not a factor for the wheezing child.
 (When there are reactions after ingesting food, the most common causes are milk, peanut products, soy, wheat, eggs.)
- Reducing exposure to viral respiratory infections may be important for the difficult-to-manage wheezer.









Many children have multiple caretakers.

All homes and caretakers should have medications, devices, and a management plan for how and when to use them.

Upper respiratory viral infections are a key precipitating factor of asthma symptoms in young children.

Primary prevention of asthma (preventing initial development) may alter its course.

- Minimize exposure to dust mites, tobacco smoke, animal dander, cockroach allergens.
 - ⇒ Exposure to high levels of dust mite and tobacco smoke are associated with an increased incidence of asthma among infants.
- Prolonged breast feeding and avoiding the early introduction of allergenic foods may reduce eczema and food sensitization, but have not been shown to reduce the prevalence of asthma.

Special concerns of the adolescent include:

- Effects of medications on appearance (height, weight, acne), ability to exercise, menses.
- Taking medications in public.
- Peer pressure.

Poorly controlled asthma may delay growth.

The potential risks of inhaled corticosteroids are well balanced by their benefits.

Adolescents

- LISTEN to the patient! Find out their expectations and goals.
- Find out what the adolescent is willing to do, and then work out a management plan together.
- Ask the adolescent about smoking, and exposure to tobacco smoke and possible drug use.
- Encourage exercise and physical activity. Asthma should not be an excuse for not participating in physical education or sports.
 - ⇒ Develop an asthma management plan that will allow them to participate in any activity that they wish.
 - ⇒ Make it easy to take medications before exercise.
- Consider symptoms related to hobbies and workplace exposures.
- Consider nonadherence if the teen is not doing well.

Asthma, inhaled corticosteroids, and linear growth

- Poorly controlled asthma may delay growth.
- Growth rates are highly variable. Short-term evaluations may not predict final adult height.
- Children with asthma tend to have longer periods of reduced growth rates before puberty (males more than females).
- Some studies of the use of inhaled corticosteroids to treat asthma in children have identified growth delay: others have not. The clinical significance of the findings is unclear. Monitoring growth is recommended.
 - ⇒ For children with mild or moderate persistent asthma, medium-dose inhaled corticosteroid therapy may be associated with a possible, but not predictable, adverse effect on linear growth.
 - ⇒ For children with severe persistent asthma, use of high-doses of inhaled corticosteroids has significantly less potential for adverse growth effects

than oral corticosteroids.

⇒ Use of spacers will minimize local and systemic effects of inhaled corticosteroids that are delivered by MDI's.

Preventing "Anticipated" Episodes of Asthma Symptoms

When you understand and recognize the triggers of asthma symptoms for a child, it is possible to prevent or at least minimize episodes of symptoms due to "anticipated exposures" to the trigger.

For "anticipated" symptoms upon exposure to:	Treat with:
Exercise	 Short-acting, inhaled beta₂-agonist, cromolyn sodium, or nedocromil sodium shortly (5-30 minutes) before exercising. Long-acting beta₂-agonist taken at least 30 minutes before exercising. Regular use of a long-term controller medication may reduce the likelihood of exercise-induced symptoms.
Cold (dry) air	 Short-acting, inhaled beta₂-agonist, cromolyn sodium, or nedocromil sodium shortly (5-30 minutes) before going out in the cold. Cover nose and mouth with a scarf on cold or windy days.
Allergens (e.g., animal dander, pollens)	Cromolyn sodium or nedocromil sodium shortly (5-30 minutes) before anticipated exposure.

Managing the child with seasonal symptoms

Some children experience asthma symptoms only in relationship to certain pollens and molds. If the child has seasonal asthma on a predictable basis, long-term control medication should be:

- Started (or increased) prior to the anticipated onset of symptoms and continued through the season, and
- Gradually decreased (or stopped) after the season.

Allergen immunotherapy may be considered for children with asthma when:

- There is clear evidence of a relationship between symptoms and exposure to an unavoidable allergen to which the child is sensitive.
- Symptoms occur all year or during a major portion of the year.
- There is difficulty controlling symptoms with pharmacologic management because multiple medications are required, medications are ineffective, or medications are not accepted by the child (or parents).

Referral to a specialist for consultation or co-management is recommended for children being considered for allergy immunotherapy. Allergen immunotherapy should be administered only in an office where facilities and trained personnel are available to treat any reaction that may occur. Life threatening reactions can occur, but are rare.

Viral upper respiratory infections are a key precipitating factor of asthma symptoms in young children.

Treating asthma symptoms due to viral upper respiratory infections (URIs)

- For mild symptoms, a short-acting, inhaled beta₂agonist (every 4 to 6 hours for 24 hours, longer with physician consult) may be sufficient to control the symptoms and to improve lung function.
- For children with recurrent URIs, when this therapy needs to be repeated more frequently than every 6 weeks, a seasonal increase in (or starting) long-term control therapy may be necessary.
- For a moderate persistent or severe persistent exacerbation, a short (3- to 10-day) course of oral corticosteroids should be considered.
- If the child has a history of severe recurrent **exacerbations with URIs,** consider initiating a short (3- to 10-day) course of oral corticosteroids at the first sign of URI.
- Appropriate long-term control therapy during the viral season may reduce the frequency and severity of viral-induced symptoms.

Managing exercise-induced asthma

- Exercise-induced bronchospasm (EIB) is caused by a loss of heat, water, or both from the airways during exercise due to hyperventilation of cool, dry air relative to the air within the lungs.
- EIB usually begins during exercise and peaks 5 to 10 minutes after stopping exercise.
- Exercise may be the only trigger of asthma for some children, particularly children with allergic rhinitis.
 - ⇒ These children should be monitored regularly because EIB is often a marker of inadequate asthma management.
- Symptoms may spontaneously resolve within 1 hour after exercise.
- A warm-up period before exercise may help.
- If asthma symptoms occur regularly with usual activities or exercise, increasing (or adding) daily longterm control medications may be warranted.
- Teachers and coaches need to be notified that a child has exercise-induced symptoms.
 - ⇒ They should be told that the child can participate in activities, but may need inhaled medication before the activity.
- Appropriate long-term control therapy, especially with anti-inflammatory medications, can reduce the frequency and severity of exercise-induced symptoms.

Exercise-induced symptoms should be anticipated in ALL children with asthma.

Asthma should not be an excuse from participating in physical education, sports, or exercise.

- Develop an asthma management plan that will allow the child to participate in any activity that they wish.
- Make it easy to take medications before exercise.
- If full activity is not possible, have the child participate to the extent that he/she can.

Sometimes physical education/activities DO need to be adjusted for the child with asthma. For example:

- On a severe allergy day
- On a windy day
- In extreme cold
- During and/or after a viral URI

Treatment for exercise-induced asthma:	Minutes before exercise to take medication:	May prevent symptoms for up to:
Short-acting inhaled beta ₂ -agonist (2-4 puffs)	5-30 (best taken just before exercising)	2-3 hours
Cromolyn sodium or nedocromil sodium (2-4 puffs)	5-30 (best taken just before exercising)	1-2 hours
Long-acting beta ₂ - agonist (2 puffs)	At least 30	10-12 hours

References

Agertoft L, Pedersen S. Importance of the inhalation device on the effect of budesonide. Arch Dis Child 1993; 69:130-133.

Ahrens R, Lux C, Bahl T, Han SH. Choosing the metered-dose inhaler spacer or holding chamber that matches the patient's need: evidence that the specific drug being delivered is an important consideration. J Allergy Clin Immunol 1995; 96:288-294.

Albazzaz MK, Neale MG, Patel KR. Dose-response study of nebulized nedocromil sodium in exercise induced asthma. Thorax 1989; 44:816-819.

Allen DB, Lemanske RF Jr. The safety of chronic asthma treatments: continuous beta agonist therapy and prolonged inhaled corticosteroids in childhood asthma. In: Middleton E Jr, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, Busse WW, eds. Allergy: Principles and Practice. 4th ed. St. Louis, MO.: Mosby Yearbook, 1993; 1-16.

Allen DB, Mullen M, Mullen B. A meta-analysis of the effect of oral and inhaled corticosteroids on growth. J Allergy Clin Immunol 1994; 93:967-976.

Allen DB. Growth suppression by glucocorticoid therapy. In: Vassallo J, ed. Endocrinology and metabolism clinics in North America. Philadelphia: W.B. Saunders Co. 1996; 699-717.

Amirav I, Newhouse MT. Metered-dose inhaler accessory devices in acute asthma: efficacy and comparison with nebulizers: a literature review. Arch Ped Adolesc Med 1997; 151:876-882.

Anderson SD. Issues in exercise-induced asthma. J Allergy Clin Immunol 1985; 76:763-772.

Balfour-Lynn L. Growth and childhood asthma. Arch Dis Child 1986; 61(11):1049-1055.

Barnes PJ, Pedersen S. Efficacy and safety of inhaled corticosteroids in asthma. Am Rev Respir Dis 1993; 148:S1-S26.

Barnes PJ. Current therapies for asthma. Promise and limitations. Chest 1997; 111:S17-S26.

Barnes PJ. From pathophysiological mechanisms to pharmacological treatment of childhood asthma. Ped Pulmonol 1995; 11:40-41.

Barnes PJ. Inhaled glucocorticoids for asthma. N Engl J Med 1995: 332:868-875.

Barros MJ, Rees PJ. Bronchodilator responses to salbutamol followed by ipratropium bromide in partially reversible airflow obstruction. Respir Med 1990; 84:371-375.

Becker AB, Simons FE. Formoterol, a new long-acting selective beta₂-adrenergic receptor agonist: double-blind comparison with salbutamol and placebo in children with asthma.

J Allergy Clin Immunol 1989; 84:891-895.

Bertelsen A, Andersen JB, Busch P, et al. Nebulized sodium cromoglycate in the treatment of wheezy bronchitis: a multicentre double-blind placebo controlled study. Allergy 1986; 41:266-270.

Bisgaard H, Munck SL, Nielsen JP, Petersen W, Ohlsson SV. Inhaled budesonide for treatment of recurrent wheezing in early childhood. Lancet 1990; 336:649-651.

Bisgaard H, Nielsen MD, Anderson B, et al. Adrenal function in children with bronchial asthma treated with beclomethasone dipropionate or budesonide. J Allergy Clin Immunol 1988; 81:1088-1095.

Bisgaard H. Use of inhaled corticosteroids in pediatric asthma. Ped Pulmonol 1997; 15:27-33.

Brogden RN, Sorkin EM. Nedocromil sodium. An updated review of its pharmacological properties and therapeutic efficacy in asthma. Drugs 1993; 45:693-715.

Bronsky EA, Kemp JP, Zhang J, Guerreiro D, Reiss TF. Dose-related protection of exercise bronchoconstriction by montelukast, a cysteinyl leukotriene-receptor antagonist, at the end of a once-daily dosing interval. Clin Pharm Thera 1997; 62:556-561.

Brown PH, Blundell G, Greening AP, Crompton GK. Do large volume spacer devices reduce the systemic effects of high dose inhaled corticosteroids? Thorax 1990; 45:736-739.

Busse WW. The role of leukotrienes in asthma and allergic rhinitis. Clin Exp Allergy 1996; 26:868-879.

Calpin C, Macarthur C, Stephens D, Feldman W, Parkin PC. Effectiveness of prophylactic inhaled steroids in childhood asthma: a systematic review of the literature. J Allergy Clin Immunol 1997; 100:452-457.

Castle W, Fuller R, Hall J, Palmer J. Serevent nationwide surveillance study: comparison of salmeterol with salbutamol in asthmatic patients who require regular bronchodilator treatment. Brit Med J 1993; 306:1034-1037.

Centers for Disease Control and Prevention. General recommendations on immunization. Morb Mortal Wkly Rep 1994; Jan 28; 43(RR-1):1-38.

Chapman KR, Verbeek PR, White JG, Rebuck AS. Effect of a short course of prednisone in the prevention of early relapse after the emergency room treatment of acute asthma. N Engl J Med 1991; 324:788-794.

Check WA, Kaliner MA. Pharmacology and pharmacokinetics of topical corticosteroid derivatives used for asthma therapy. Am Rev Respir Dis 1990; 141:S44-S51.

Clark B. General pharmacology, pharmacokinetics, and toxicology of nedocromil sodium. J Allergy Clin Immunol 1993; 92:200-202.

Clark CE, Ferguson AD, Siddorn JA. Respiratory arrests in young asthmatics on salmeterol. Respir Med 1993; 87(3):227-228.

Clark DJ, Clark RA, Lipworth BJ. Adrenal suppression with inhaled budesonide and fluticasone propionate given by large volume spacer to asthmatic children. Thorax 1996; 51:941-943.

Clissold SP, Heel RC. Budesonide: A preliminary review of its pharmacodynamic properties and therapeutic efficacy in asthma and rhinitis. Drugs 1984; 28:485-518.

Cockcroft DW, Murdock KY. Comparative effects of inhaled salbutamol, sodium cromoglycate, and beclomethasone dipropionate on allergen-induced early asthmatic responses, late asthmatic responses, and increased bronchial responsiveness to histamine. J Allergy Clin Immunol 1987; 79:734-740.

Cockcroft DW, O'Byrne PM, Swystun VA, Bhagat R. Regular use of inhaled albuterol and the allergen induced late asthmatic response. J Allergy Clin Immunol 1995; 96:44-49.

Connett GJ, Warde C, Wooler E, Lenney W. Use of budesonide in severe asthmatics aged 1-3 years. Arch Dis Child 1993; 69:351-355.

Creticos P, Burk J, Smith L, et al. The use of twice daily nedocromil sodium in the treatment of asthma. J Allergy Clin Immunol 1995; 95:829-836.

Crompton G, Duncan J. Clinical assessment of a new breath-actuated inhaler. Practitioner 1989; 233:268-269.

D'Alonzo GE, Nathan RA, Henochowicz S, et al. Salmeterol xinafoate as maintenance therapy compared with albuterol in patients with asthma. J Am Med Assoc 1994; 271:1412-1416.

Dahlen B, Zetterstrom O, Bjorck T, Dahlen SE. The leukotrieneantagonist IC:204, 219 inhibits the early airway reaction to cumulative bronchial challenge with allergen in atopic asthmatics. Eur Respir J 1994; 7:324-331.

de Benedictis FM, Tuteri G, Pazzelli P, et al. Cromolyn versus nedocromil: duration of action in exercise-induced asthma in children. J Allergy Clin Immunol 1995; 96:510-514.

Djukanovic R, Wilson TW, Britten KM, et al. Effect of an inhaled corticosteroid on airway inflammation and symptoms of asthma. Am Rev Respir Dis 1992; 145:669-674.

Doull IJM, Freezer NJ, Holgate ST. Growth of prepubertal children with mild asthma treated with inhaled beclomethasone dipropionate. Am J Respir Crit Care Med 1995; 151:1717-1719.

Drazen JM, Israel E. Treatment of chronic stable asthma with drugs active on the 5-lipoxygenase pathway. Int Arch Allergy Immunol 1995; 107:319-320.

Eady RP. The pharmacology of nedocromil sodium. Eur J Respir Dis 1986; 147:S112-S119.

Eisen SA, Miller DK, Woodward RS, Spitznagel E, Przybeck TR. The effect of prescribed daily dose frequency on patient medication compliance. Arch Intern Med 1990; 150(9): 1881-1884.

Estelle F, Simmons R. A comparison of beclomethasone, salmetherol, and placebo in children with asthma. N Engl J Med 1997; 337:1659-1665.

Everard ML, Clark AR, Milner AD. Drug delivery from holding chambers with attached facemask. Arch Dis Child 1992; 67:580-585.

Fabbri LM, Piattella M, Caramori G, Ciaccia A. Oral vs inhaled asthma therapy: pros, cons and combinations. Drugs 1996; 52(S6):20-28.

Fiocchi A, Riva E, Santini I, et al. Effect of nedocromil sodium on bronchial hyperreactivity in children with nonatopic asthma. Ann Allergy Asthma Immunol 1997; 79:503-506.

Fish JE, Kemp JP, Lockey RF, et al. Zafirlukast for symptomatic mild-to-moderate asthma: a 13-week multicenter study. The Zafirlukast Trialists Group. Clin Ther 1997; 19:675-690.

Fitzpatrick MF, Mackay T, Driver H, Douglas NJ. Salmeterol in nocturnal asthma: a double blind, placebo controlled trial of a long acting inhaled beta₂-agonist. Brit Med J 1990; 301: 1365-1368.

Fuglsand G, Pedersen S. Comparison of Nebuhaler and nebulizer treatment of acute severe asthma in children. Eur J Respir Dis 1986; 69:109-113.

Gaddy JN, Margolskee DJ, Bush RK, Williams VC, Busse WW. Bronchodilation with a potent and selective leukotriene D_4 (LTD₄) receptor antagonist (MK-571) in patients with asthma. Am Rev Respir Dis 1992; 146(2): 358-363.

Geller M. Acute management of severe childhood asthma. AACN Clin Issues 1996; 7:519-0528.

Geller-Berstein C, Sneh N. The management of bronchial asthma in children under the age of 3 years using Intal (sodium cromoglycate) administered by Spinhaler. Clin Allergy 1980; 10:503-508.

Gemou-Engesaeth V, Bush A, Kay AB, Hamid Q, Corrigan CJ. Inhaled glucocorticoid therapy of childhood asthma is associated with reduced peripheral blood t-cell activation and 'TH -type' cytokine mRNA expression. Pediatrics 1997; 99:695-703.

Glass J, Archer LN, Adams W, Simpson H. Nebulised cromoglycate, theophylline, and placebo in preschool asthmatic children. Arch Dis Child 1981; 56:648-651.

Gleeson JG, Price JF. Controlled trial of budesonide given by the nebuhaler in preschool children with asthma. Brit Med J 1988; 297:163-166.

Goldstein DE, Konig P. Effect of inhaled beclomethasone dipropionate on hypothalamic-pituitary-adrenal axis function in children with asthma. Pediatrics 1983; 72:60-64.

Gonzalez JP, Brogden RN. Nedocromil sodium. A preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in the treatment of reversible obstructive airways disease. Drugs 1987; 34:560-577.

Goodman DC, Littenberg B, O'Connor GT, Brooks JG. Theophylline in acute childhood asthma: a meta-analysis of its efficacy. Ped Pulmonol 1996; 21:211-218.

Goodwin A. Asthma therapy-Treating childhood asthma with nebulised steroids. Professional Care of Mother & Child 1995; 5:7-9.

Goren A, Noviski N, Avital A, et al. Assessment of the ability of young children to use a powder inhaler device (Turbuhaler). Pediatr Pulmonol 1994; 18:77-80.

Green CP, Price JF. Prevention of exercise induced asthma by inhaled salmeterol xinafoate. Arch Dis Child 1992; 67: 1014-1017.

Gross NJ. Ipratropium bromide. N Engl J Med 1988; 319: 486-494.

Gustafsson P, Tsanakas J, Gold M, et al. Comparison of the efficacy and safety of inhaled fluticasone 200 mcg/day with inhaled beclomethasone dipropionate 400 mcg/day in mild and moderate asthma. Arch Dis Child 1993; 69:206-211.

Haahtela T, Jarvinen M, Kava T, et al. Comparison of a beta - agonist, terbutaline, with an inhaled corticosteroid, budesorfide, in newly detected asthma. N Engl J Med 1991; 325:388-392.

Haahtela T, Jarvinen M, Kava T, et al. Effects of reducing or discontinuing inhaled budesonide in patients with mild asthma. N Engl J Med 1994; 331:700-705.

Hanania NA, Wittman R. Kesten S. Chapman KR. Medical personnel's knowledge of and ability to use inhaling devices. Metered-dose inhalers, spacing chambers, and breath-actuated dry powder inhalers. Chest 1994; 105(1):111-116.

Hansen-Flaschen J, Schotland H. New treatments for exercise-induced asthma. N Engl J Med 1998; 339:129-3.

Harding SM. The human pharmacology of fluticasone propionate. Respir Med 1990; 84(Suppl A):25-29.

Hendeles L, Harman E, Huang D, et al. Theophylline attenuation of airway responses to allergen: comparison with cromolyn metered-dose inhaler. J Allergy Clin Immunol 1995; 95:505-514.

Henderson WR Jr. The role of leukotrienes in inflammation. Ann Intern Med 1994; 121:684-697.

Henriksen JM, Agertoft L, Pedersen S. Protective effect and duration of action of inhaled formoterol and salbutamol on exercise-induced asthma in children. J Allergy Clin Immunol 1992; 89:1176-1182.

Higgins RM, Cookson W, Lane DJ, et al. Cardiac arrythmias caused by nebulized beta-agonist therapy. Lancet 1987; 2:863-864.

Hilman BC, Bairnsfather L, Washburne W, Vekovius AL. Nebulized cromolyn sodium: safety, efficacy, and role in the management of childhood asthma. Ped Allergy Immunol 1987; 1:43-52.

Holgate ST, Bradding P, Sampson AP. Leukotriene antagonists and synthesis inhibitors: new directions in asthma therapy. J Allergy Clin Immunol 1996; 98:1-13.

Holgate ST, Frew AJ, Choosing therapy for childhood asthma. N Engl J Med 1997; 337:1690-1692.

Horwitz RJ, McGill KA, Busse WW. The role of leukotriene modifiers in the treatment of asthma. Am J Respir Crit Care Med 1998:157:1363-1371.

llangovan P, Pedersen S, Godfrey S, Nikander K, Noviski N, Warner JO. Treatment of severe steroid dependent preschool asthma with nebulised budesonide suspension. Arch Dis Child 1993; 68:356-359.

Ind PW. Anti-leukotriene intervention: is there adequate information for clinical use in asthma? Respir Med 1996; 90:575-586.

Jones AH, Langdon CG, Lee PS, et al. Pulmicort Turbuhaler once daily as initial prophylactic therapy for asthma. Respir Med 1994; 88:293-299.

Kamada AK, Hill MR, Ikle DN, Brenner AM, Szefler SJ. Efficacy and safety of low-dose troleandomycin therapy in children with severe, steroid-requiring asthma. J Allergy Clin Immunol 1993; 91:873-882.

Kamada AK, Szefler SJ. Glucocorticoids and growth in asthmatic children. Pediatr Allergy Immunol 1995; 6:145-154.

Kasper WJ, Howe PM. Fatal varicella after a single course of corticosteroids. Pediatr Infect Dis J 1990; 9:729-732.

Kelly HW. Asthma pharmacotherapy: current practices and outlook. Pharmacotherapy 1997; 17(1 Pt 2):S13-S21.

Kemp JP, Dockhorn RJ, Busse WW, Bleecker ER, Van As A. Prolonged effect of inhaled salmeterol against exercise-induced bronchospasm. Am J Respir Crit Care Med 1994; 150: 1612-1615.

Kemp JP, Furukawa CT, Bronsky EA, et al. Albuterol treatment for children with asthma: a comparison of inhaled powder and aerosol. J Allergy Clin Immunol 1989; 83:697-702.

Kerem E, Levison H, Schuh S, et al. Efficacy of albuterol administered by nebulizer versus spacer device in children with acute asthma. J Pediatr 1993; 123:313-317.

Kerrebijn KF, van Essen-Zandvliet EE, Neijens HJ. Effect of longterm treatment with inhaled corticosteriods and beta-agonists on the bronchial responsiveness in children with asthma. J Allergy Clin Immunol 1987; 79(4):653-659.

Kerstjens HA, Brand PL, Hughes MD, et al. A comparison of bronchodilator therapy for obstructive airways disease. N Engl J Med 1992; 327:1413-1419.

Kim CS, Eldridge MA, Sackner MA. Oropharyngeal deposition and delivery aspects of metered-dose inhaler aerosols. Am Rev Respir Dis 1987; 135:157-164.

Konig P, Eigen H, Ellis MH, et al. The effect of nedocromil sodium on childhood asthma during the viral season. Am J Respir Crit Care Med 1995; 152:1879-1886.

Konig P, Shaffer J. The effect of drug therapy on long-term outcome of childhood asthma: a possible preview of the international guidelines. J Allergy Clin Immunol 1996; 98:1103-1111.

Laitinen LA, Laitinen A, Haahtela T. A comparative study of the effects of an inhaled corticosteroid, budesonide, and a beta - agonist, terbutaline, on airway inflammation in newly diagnosed asthma: a randomized, double-blind, parallel-group controlled trial. J Allergy Clin Immunol 1992; 90:32-42.

Laitinen LA, Laitinen A, Heino M, Haahtela T. Eosinophilic airway inflammation during exacerbation of asthma and its treatment with inhaled corticosteroid. Am Rev Respir Dis 1991; 143(2):423-427.

Lantner RR, Ros SP. Emergency management of asthma in children: impact of NIH guidelines. Ann Allergy Asthma Immunology 1995; 74:188-191.

Leff JA, Busse WW, Pearlman D, et al. Montelukast, a leukotriene-receptor antagonist, for the treatment of mild asthma and exercise-induced bronchoconstriction. N Engl J Med 1998; 339:147-52.

Lemanske RF, Allen DB. Choosing a long-term controller medication in childhood asthma. The proverbial two-edged sword. Am J Respir Crit Care Med 1997; 156:685-687.

Lenney W, Pedersen S, Boner AL, et al. Efficacy and safety of salmeterol in childhood asthma. Eur J Ped 1995; 154:983-990.

Leversha AM, Asher MI. Update on spacer devices in childhood asthma. N Zealand Med J 1996; 109:76-78.

Levy J, Zalkinder I, Kuperman O, et al. Effect of prolonged use of inhaler use of inhaled steroids on the cellular immunity of children with asthma. J Allergy Clin Immunol 1995; 95:806-812.

Li JTC, Reed C. Do recent findings warrant a change in approach? Inhaled beta-agonists: weighing risks and benefits. J Respir Dis 1993; 14(9):991-1009.

Lipworth BJ. New perspectives on inhaled drug delivery and systemic bioactivity. Thorax 1995; 50:105-110.

Liu MC, Dube LM, Lancaster J. Acute and chronic effects of a 5-lipoxygenase inhibitor in asthma: a 6-month randomized multicenter trial. J Allergy Clin Immunol 1996; 98:859-871.

Lundback B, Rawlinson DW, Palmer JB. Twelve-month comparison of salmeterol and salbutamol as dry powder formulations in asthmatic patients. European Study Group. Thorax 1993; 48(2):148-153.

McFadden ER Jr, Gilbert IA. Exercise-induced asthma. N Engl J Med 1994; 330:1362-1367.

McGill KA, Busse WW. Zileuton. Lancet 1996; 348:519-524.

McGill KA, Joseph B, Busse WW. Corticosteroids in the treatment of asthma. Practical recommendations. Clin Immunother 1995; 4:16-48.

Meltzer SS, Hasday JD, Cohn J, Bleecker ER. Inhibition of exercise-induced bronchospasm by zileuton: a 5-lipoxygenase inhibitor. Am J Respir Crit Care Med 1996; 153:931-935.

Miraglia del Giudice, Capristo A, Maiello, Apuzzo G. Nebulized sodium cromoglycate for the treatment of asthma in children under five years of age. Mod Probl Paediat 1982; 21:122-127.

Mollman H, Rohdewald P, Schmidt EW, Salomon V, Derendorf H. Pharmacokinetics of triamcinolone acetonide and its phosphate ester. Eur J Clin Pharmacol 1985; 29:85-89.

Mullen ML, Mullen B, Carey M. The association between beta₂-agonist use and death from asthma. J Am Med Assoc 1993; 270:1842-1845.

Munoz NM, Douglass I, Mayer D, et al. Eosinophil chemotaxis inhibited by 5-lipoxygenase blockade and leukotriene receptor antagonism. Am J Respir Crit Care Med 1997; 155:1398-1403.

Nassif EG, Weinberger M, Thompson R, Huntley W. The value of maintenance theophylline in steroid dependent asthma. N Engl J Med 1981; 304:71-75.

Nastasi KJ, Heinly TL, Blaiss MS. Exercise-induced asthma and the athlete. J Asthma 1995; 32:249-257.

Nathan RA. Anti-leukotriene agents: a new direction in asthma therapy. J Asthma 1996; 33(6):353-366.

Nelson HS, Hamilos DL, Corsello PR, et al. A double-blind study of troleandomycin and methylprednisolone in asthmatic subjects who require daily corticosteroids. Am Rev Respir Dis 1993; 147:398-404.

Nelson HS, Weber RW. Endocrine aspects of allergic diseases. In: Bierman CW, Pearlman DS, eds. Allergic diseases from infancy to adulthood. Philadelphia: WB Saunders, 1988; 15.

Nelson JA, Strauss L, Skowronski M, et al. Effect of long-term salmeterol treatment on exercise-induced asthma. N Engl J Med 1998; 339:141-146.

Newhouse MT, Dolovich MB. Control of asthma by aerosols. N Engl J Med 1986; 315:870-874.

Newhouse MT, Ruffin RE. Deposition and fate of aerosolized drugs. Chest 1978; 73(S6):936-943.

Newman SP, Millar AB, Lennard-Jones TR, Moren F, Clarke SW. Improvement of pressurized aerosol deposition with Nebuhaler spacer device. Thorax 1984; 39:935-941.

Newman SP, Moren F, Pavla D, Little F, Clarke SW. Deposition of pressurized suspension aerosols inhaled through extension devices. Am Rev Respir Dis 1981; 124:317-320.

Newman SP, Weisz AWB, Talaee N, Clarke SW. Improvement of drug delivery with a breath actuated pressurised aerosol for patients with poor inhaler technique. Thorax 1991; 46:712-716.

Ninan TK, Russell G. Asthma, inhaled corticosteroid treatment, and growth. Arch Dis Child 1992; 67(6):703-705.

Noonan M, Chervinsky P, Busse WW, et al. Fluticasone propionate reduces oral prednisone use while it improves asthma control and quality of life. Am J Respir Crit Care Med 1995; 152:1467-1473.

Novembre G, Frongia GF, Veneruso G, Vierucci A. Inhibition of exercise-induced asthma (EIA) by nedocromil sodium and sodium cromoglycate in children. Pediatr Allergy Immunol 1994; 5:107-110.

O'Byrne PM. Exercise-induced bronchoconstriction: elucidating the roles of leukotrienes and prostaglandins. Pharmacotherapy 1997; 17(1 pt 2):31S-38S.

O'Callaghan C, Cant M, Robertson C. Delivery of beclomethasone dipropionate from a spacer device: what dose is available for inhalation? Thorax 1994; 49:961-964.

O'Hickey SP, Rees PJ. High-dose nedocromil sodium as an addition to inhaled corticosteroids in the treatment of asthma. Respir Med 1994; 88:499-502.

Oliveira CAA, Solé D, Naspitz CK, Rachelefsky GS. Improvement of bronchial hyperresponsiveness in asthmatic children treated for concomitant sinusitis. Ann Allergy Asthma Immunol 1997; 79:70-74.

Pachter LM, Cloutier MM, Bernstein BA. Ethnomedical (folk) remedies for childhood asthma in a main-land Puerto Rican community. Arch Pediatr Adolesc Med 1995; 149:982-988.

Pauwels RA, Joos GF, Kips JC. Leukotrienes as therapeutic target in asthma. Allergy 1995; 50:615-622.

Pauwels RA. New aspects of the therapeutic potential of theophylline in asthma. J Allergy Clin Immunol 1989; 83:548-553.

Pearlman DS, Chervinsky P, LaForce C, et al. A comparison of salmeterol with albuterol in the treatment of mild-to-moderate asthma. N Engl J Med 1992; 327:1420-1425.

Pedersen S, Fuglsang G. Urine cortisol excretion in children treated with high doses of inhaled corticosteroids: a comparison of budesonide and beclomethasone. Eur Respir J 1988; 1:433-435.

Pedersen S, Hansen OR, Fuglsang G. Influence of inspiratory flow rate upon the effect of a Turbuhaler. Arch Dis Child 1990; 65:308-310.

Pedersen S, Hansen OR. Budesonide treatment of moderate and severe asthma in children: a dose-response study. J Allergy Clin Immunol 1995; 95:29-33.

Pedersen S, Mortensen S. Use of different inhalation devices in children. Lung 1990; 168:S653-S657.

Petersen W, Karup-Pedersen F, Friis B, et al. Sodium cromoglycate as a replacement for inhaled corticosteroids in mild-to-moderate childhood asthma. Allergy 1996; 51:870-875.

Pincus DJ, Szefler SJ, Ackerson LM, Martin RJ. Chronotherapy of asthma with inhaled steroids: the effect of dosage timing on drug efficacy. J Allergy Clin Immunol 1995; 95:1172-1178.

Prahl P, Jensen T, Bjerregaard-Andersen H. Adrenocortical function in children on high-dose steroid aerosol therapy. Allergy 1987; 42:541-544.

Prahl P, Jenson T. Decreased adrenocortical suppression utilizing the nebuhaler for inhalation of steroid aerosols. Clin Allergy 1987; 17:393-398.

Prahl P. Adernocortical suppression following treatment with beclomethasone dipropionate and budesonide. Clin Exp Allergy 1991; 21:145-146.

Ramage L, Lipworth BJ, Ingram CG, Cree IA, Dhillon DP. Reduced protection against exercise induced bronchoconstriction after chronic dosing with salmeterol. Respir Med 1994; 88(5):363-368.

Reisman J, Galdes-Sebalt M, Kazim F, Canny G, Levison H. Frequent administration by inhalation of salbutamol and ipratropium bromide, in the initial management of severe acute asthma in children. J Allergy Clin Immunol 1988; 81:16-20.

Reiss TF, Altman LC, Chervinsky P, et al. Effects of montelukast (MK-0476); a new potent cysteinyl leukotriene (LTD4) receptor antagonist, in patients with chronic asthma. J Allergy Clin Immunol 1996; 98;528-534.

Reiss TF, Sorkness CA, Stricker W, et al. Effects of montelukast (MK-0476) - a potent cysteinyl leukotriene receptor antagonist on bronchodilation in asthmatic subjects treated with and without inhaled corticosteriods. Thorax 1997; 52:45-48.

Risser AL, Mazur LJ. Use of folk remedies in a Hispanic population. Arch Pediatr Adolesc Med 1995; 149:978-981. Rooklin AR, Lampert SI, Jaeger EA, McGeady SJ, Mansmann HC Jr. Posterior subcapsular cataracts in steroid-requiring asthmatic children. J Allergy Clin Immunol 1979; 63(6):383-386.

Rubin BK, Albers GM. Use of anticholinergic bronchodilation in children. Am J Med 1996; 100:49s-53s.

Ruggins NR, Milner AD, Swarbrick A. An assessment of a new breath-actuated inhaler device in acutely wheezy children. Arch Dis Child 1993; 68:477-480.

Scalabrin DM, Naspitz CK. Efficacy and side effects of salbutamol in acute asthma in children: comparison of oral route and two different nebulizer systems. J Asthma 1993; 30:51-59.

Scarfone RJ, Fuchs SM, Nager AL, Shane SA. Controlled trial of oral prednisone in the emergency department treatment of children with acute asthma. Pediatrics 1993; 2:513-518.

Schnecker MH, Wilson AF, Mukai DS, et al. A device for overcoming discoordination with metered-dose inhalers. J Allergy Clin Immunol 1993; 92:783-789.

Schuh S, Johnson DW, Callahan S, Canny G, Levison H. Efficacy of frequent nebulized ipratropium bromide added to frequent high-dose albuterol therapy in severe childhood asthma. J Pediatr 1995; 126:639-645.

Schwartz HJ, Petty T, Dube LM, et al. A randomized controlled trial comparing zileuton with theophylline in moderate asthma. Arch Int Med 1998; 158:141-148.

Sears MR. The relationship between beta-agonists and asthma mortality. J Asthma Allergy Pediatr 1993; 6:123-128.

Selroos O, Halme M. Effect of a volumatic spacer and mouth rinsing on systemic absorption of inhaled corticosteroids from a metered dose inhaler and dry powder inhaler. Thorax 1991; 46:891-894.

Shapiro GG, Konig P. Cromolyn sodium: a review. Pharmacotherapy 1985; 5:156-170.

Shaw NJ, Edmunds AT. Inhaled beclomethasone and oral candidiasis. Arch Dis Child 1986; 61:788-790.

Silverman M, Connolly NM, Balfour-Lynn L, Godfrey S. Long-term trial of disodium cromoglycate and isoprenaline in children with asthma. Brit Med J 1972; 3:378-381.

Silverstein MD, Yunginger JW, Reed CE, et al. Attained adult height after childhood asthma: effect of glucocorticoid therapy. J Allergy Clin Immunol 1997; 99:466-474.

Simons FE, Persaud MP, Gillespie CA, Cheang M, Shuckett EP. Absence of posterior subcapsular cataracts in young patients treated with inhaled glucocorticoids. Lancet 1993; 342: 776-778.

Sorkness CA. The use of 5-lipoxygenase inhibitors and leukotriene receptor antagonists in the treatment of chronic asthma. Pharmacotherapy 1997; 17:50S-54S.

Spector SL, Smith LJ, Glass M. Effects of 6 weeks of therapy with oral doses of ICl 204, 219, a leukotriene D_4 receptor antagonist, in subjects with bronchial asthma. Am J Respir Crit Care Med 1994; 150:618-623.

Spitzer WO, Suissa S, Ernst P, et al. The use of beta-agonist and the risk of death and near death from asthma. N Engl J Med 1992; 326:501-506.

Stoloff SW. The changing role of theophylline in pediatric asthma. Am Fam Phys 1994; 49:839-844.

Storms WW, Bodman SF, Nathan RA, et al. Use of ipratropium bromide in asthma. Am J Med 1986; 81:61-66.

Strauss RE, Wertheim DL, Bonagura VR, Valacer DJ. Aminophylline therapy does not improve outcome and increases adverse effects in children hospitalized with acute asthmatic exacerbations. Pediatrics 1994; 93:205-210.

Strunk RC, Mrazek DA, Wolfson-Fuhrman GS, LaBrecque JF. Physiological and psychological characteristics associated with deaths due to asthma in childhood. A case-controlled study. J Am Med Assoc 1985; 254:1193-1198.

Suissa S, Dennis R, Ernst P, Sheehy O, Wood-Dauphinee S. Effectiveness of the leukotriene receptor antagonist zafirlukast for mild-to-moderate asthma. A randomized, double-blind, placebo-controlled trial. Ann Inter Med 1997; 126:177-183.

Suissa S, Ernst P, Boivin JP, et al. A cohort analysis of excess mortality in asthma and the use of inhaled beta-agonists. Am J Respir Crit Care Med 1994; 149:604-610.

Sullivan P. Bekir S, Jaffar Z, et al. Anti-inflammatory effects of low-dose oral theophylline in atopic asthma. Lancet 1994; 343:1006-1008.

Svendsen UG, Jorgensen H. Inhaled nedocromil sodium as additional treatment to high dose inhaled corticosteroids in the management to bronchial asthma. Eur Respir J 1991; 4:992-999.

Szefler SJ, Bender BG, Jusko WJ, et al. Evolving role of theophylline for treatment of chronic childhood asthma. J Ped 1995; 127:176-185.

Szefler SJ. Glucocorticoid therapy for asthma: clinical pharmacology. J Allergy Clin Immunol 1991; 88:147-165.

Tabachnik E, Zadik Z. Clinical and laboratory: diurnal cortisol secretion during therapy with inhaled beclomethasone dipropionate in children with asthma. J Pediatr 1991; 118:294-297.

Tasche MJA, van der Wouden JC, Uijen JHJM, et al. Randomised placebo-controlled trial of inhaled sodium cromoglycate in 1-4 year old children with moderate asthma. Lancet 1997; 350:1060-1064.

Thorsson L, Edsbacker S, Conradson TB. Lung deposition of budesonide from Turbuhaler is twice that from a pressurized metered-dose inhaler P-MDI. Eur Respir J 1994; 7:1839-1844.

Tinkelman DG, Reed CE, Nelson HS, Offord KP. Aerosol beclomethasone dipropionate compared with theophylline as primary treatment of chronic, mild to moderately severe, asthma in children. Pediatrics 1993; 92:64-77.

Tomac N, Tuncer A, Saraclar Y, Adalioglu G. Efficacy of salmeterol in the treatment of childhood asthma. Acta Paediatrica Japonica 1996; 38:498-494.

Toogood JH, Jennings B, Greenway RW, Chuang L. Candidiasis and dysphonia complicating beclomethasone treatment of asthma. J Allergy Clin Immunol 1980; 65:145-153.

Tullett WM, Tan KM, Wall RT, Patel KR. Dose-response effect of sodium cromoglycate pressurized aerosol in exercise induced asthma. Thorax 1985; 40:41-44.

Turpeinen M, Sorva R, Juntunen-Backman K. Changes in carbohydrate and lipid metabolism in children with asthma inhaling budesonide. J Allergy Clin Immunol 1991; 88:384-389.

Van Beever HP, Stevens WJ. Pharmacotherapy of childhood asthma. An inflammatory disease. Drugs 1992; 44:36-46.

van Essen-Zandvliet EE, Hughes MD, Waalkens HJ, et al. Effects of 22 months of treatment with inhaled corticosteroids and/or beta -agonists on lung function, airway responsiveness, and symptoms in children with asthma. Am Rev Respir Dis 1992; 146:547-554.

Verberne AAPH, Frost C, Duiverman EJ, et al. Addition of salmeterol versus doubling the dose of beclomethasone in children with asthma. Am J Respir Crit Care Med 1998; 158:213-219.

Verberne AAPH, Frost C, Roorda RJ, et al. One-year treatment with salmeterol compared with beclomethasone in children with asthma. Am J Respir Crit Care Med 1997; 156:688-965.

Vidgren M, Kärkkäinen A, Karjalainen P, Nuutinen J, Paronen P. In vitro and in vivo deposition of drug particles from pressurized aerosol and dry powder inhaler. Drug Devel Indust Pharm 1983; 14:2649-2665.

Waalkens HJ, Van Essen-Zandvliet EE, Hughes MD, et al. Cessation of long-term treatment with inhaled corticosteroid (budesonide) in children with asthma results in deterioration. Am Rev Respir Dis 1993; 148:1252-1257.

Weber RW. Role of long-acting beta₂-agonists in asthma. Ann Allergy 1992; 69:381-384.

Wechsler ME, Garpestad E, Flier SR, et al. Theophylline in asthma. N Engl J Med 1996; 334:1380-1388.

Wennergren G, Sigurdur K, Strannegärd IL. Decrease in hospitalization for treatment of childhood asthma with increased use of antiinflammatory treatment, despite an increase in the prevalence of asthma. J Allergy Clin Immunol 1996; 97:742-748.

Wenzel SE, Kamada AK. Zileuton: the first 5-lipoxygenase inhibitor for the treatment of asthma. Ann Pharmacother 1996: 30:858-864.

Wilson NM, Silverman M. Treatment of acute, episodic asthma in preschool children using intermittent high dose inhaled steroids at home. Arch Dis Child 1990; 65:407-410.

Wolthers OD. Long-, intermediate- and short-term growth studies in asthmatic children treated with inhaled glucocorticosteroids. Eur Respir J 1996; 9:821-827.

Woolcock A, Lundback B, Ringdal N, Jacques LA. Comparison of addition of salmeterol to inhaled steroids with doubling of the dose of inhaled steroid. Am J Respir Crit Care Med 1996; 153:1481-1488.

Woolley M, Anderson SD, Quigley BM. Duration of terbutaline sulfate and cromolyn sodium alone and in combination on exercise-induced asthma. Chest 1990; 97:39-45.

Wright RO, Santucci KA, Jay GD, Steels DW. Evaluation of preand post-treatment pulse oximetry in acute childhood asthma. Acad Emerg Med 1997; 4:114-117.

Wurthwein G, Rohdewald P. Activation of beclomethasone dipropionate by hydrolysis to beclomethasone-17monopropionate. Biopharm Drug Dispos 1990; 11:381-394.

Yates DH, Sussman HS, Shaw MJ, Barnes PJ, Chung KF. Regular formoterol treatment in mild asthma. Effect on bronchial responsiveness during and after treatment. Am J Respir Crit Care Med 1995; 152:1170-1174.

Zachary CT, Evans R III. Perioperative management for childhood asthma. Ann Allergy Asthma Immunol. 1996; 77:468-474.

Zhao JJ, Rogers JD, Holland SD, et al. Pharmacokinetics and bioavailabilty of montelukast sodium (MK-0476) in healthy young and elderly volunteers. Biopharm Drug Dispos 1997; 18:796-777.

Ziment I, Stein M. Inappropriate and unusual remedies. In: Weiss EB, Stein M, eds. Bronchial Asthma. Boston: Little, Brown and Company, 1993; 1145-1151.